Applicants: Young-Choon Moon
Application No.: 10/799,507

REMARKS

The Claim Amendments

Applicant has amended claims 1, 4 and 5 to recite that Ring A is optionally substituted with the listed substituents. Support may be found in the definition of R^1 in originally-filed claim 1 and throughout the specification as filed.

Applicant has amended claim 6 to correct its dependency. Applicant has amended claims 9 and 19 to delete compound I-9. Applicant has further amended claim 19 to correct its dependency and to recite a composition comprising said compound. Applicant has amended claim 10 to be additionally dependent from claims 21 and 22. Applicant has canceled claim 16. Applicant has amended claim 17 to claim a method of treating or lessening the severity of diabetes, and has amended claims 11 and 20 to recite a composition or method comprising an additional therapeutic agent for treating diabetes. Applicant has further amended claim 20 to be dependent from claim 19. Support for these amendments may be found in the specification and in the claims as originally filed.

None of these amendments adds new matter. Their entry is requested.

Applicant reserves the right to pursue canceled subject matter in this application or in future continuing or divisional applications.

The Response

The Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 16-17 and 19-20 under 35 U.S.C. §112, first paragraph. The Examiner states that the specification, while being enabling for a method of treatment of stroke, does not reasonably provide enablement for a method of inhibiting the activity of various receptors recited in the claims or treating or lessening the severity of diseases or conditions recited in the claims. The Examiner states that there are complex interactions that contribute to the carcinogenic process and that "rigorously planned and executed clinical trials . . . are critical for selecting the optimal dose and schedule."

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Applicant respectfully disagrees with the Examiner's rejection, but has canceled claim 16 and amended claim 17 to expedite prosecution. Amended claim 17 recites a method of treating or lessening the severity of diabetes, while amended claim 20 recites the additional step of administering an additional therapeutic for treating diabetes. These claims are clearly enabled by the specification. In particular, the specification teaches methods of administering GSK-3 inhibitors of the invention (see, e.g., [0062] to [0072] on pages 24-27). The specification also discloses that the GSK-3 inhibitors of the invention may be used to treat diabetes (see, e.g., [0076] and [0077] on pages 28-29). Further, the specification teaches various additional therapeutic agents that can be used to treat diabetes, including insulin, glitazones and sulfonyl ureas (see, e.g., [0081] on page 29-30). Thus, the specification as originally filed fully enables the claimed invention.

The use of GSK-3 inhibitors to treat diabetes was also well established at the time the invention was made in a well-known *in vivo* animal model of diabetes. Cline et al., *Diabetes* 51: 2903-2910, 2002 (hereafter "Cline") disclosed that a GSK-3 inhibitor treatment activated glycogen synthase activity in the Zucker diabetic fatty (ZDF) rat model of diabetes, which significantly improved oral glucose disposal and significantly lowered fasting plasma glucose in diabetic rats (see, e.g., page 2909, right column). Similarly, Henriksen et al., *J. Physiol. Endocrinol. Metab.* 284: E892-E900, 2003 (hereafter "Henriksen") showed that administration of a GSK-3 inhibitor to insulin-resistant diabetic ZDF rats improved whole body glucose disposal and insulin sensitivity (see, e.g., page E899, right column). Taken together with the specification, Cline and Henricksen clearly show that there is a reasonable correlation between the GSK-3 inhibitors of the invention, the *in vitro* data showing their GSK-3 inhibitory activity, and the use of these compounds to treat diabetes.

Further, contrary to the Examiner's assertion, clinical trials identifying an "optimal dose and schedule" are not required for patentability. "[I]t is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation." See, e.g., Manual of

Patent Examining Procedure (MPEP) §2164.01(c). In this case, a skilled artisan would be able to discern an appropriate dosage and method of use based upon the information provided in the specification along with the general knowledge of one skilled in the art.

The Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner states that claims 9 and 19 are indefinite because they allegedly fail to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that compound I-9 lacks insufficient antecedent basis in claims 1 or claims 16-18 on which claims 9 and 19 are dependent.

Applicant has canceled compound I-9 from claims 9 and 19, thus obviating this rejection.

The Rejections Under 35 U.S.C. §102

The Examiner has rejected claims 1, 2, 4, 5 and 10 as allegedly being anticipated by Mittelbach et al., CAPLUS Abstract 92:146395. The Examiner asserts that the limitation that "when ring A is phenyl, it must be substituted" is not sufficient to remove the reference compound because the phenyl can be substituted with R^1, which can be hydrogen.

Applicant has amended claims 1, 2, 4, 5 and 10 such that R^1 cannot be H, thus obviating this rejection.

The Examiner has rejected claims 1, 2, 4, 5, 10, 11, 16-18 and 20 as allegedly being anticipated by Adam et al., EP 1 074 549 (hereafter "the '549 patent"). The Examiner states that ring A is an aryl ring that is optionally substituted with 1-4 substituents, wherein two substituents taken together with the atoms to which they are attached may form a 3-8 membered ring. The Examiner further states that the '549 patent teaches that the compounds are useful in the treatment of stroke, Alzheimer's disease, Parkinson's disease, etc. Applicant traverses.

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Ring A is defined in independent claims 1, 17 and 18, from which claims 2, 4, 5, 10, 11 and 20 variously depend, as being a 5-6 membered aryl, heterocyclyl or heteroaryl ring and is shown in formula I to be directly linked to the 1,6-dihydro-pyrimidine-5-carbonitrile. Thus, when two substituents on ring A are taken together to form a 3-8 membered ring, the 3-8 membered ring must be fused to the 5-6 membered aryl, heterocyclyl or heteroaryl ring and not directly attached to the 1,6-dihydropyrimidine-5-carbonitrile. This interpretation is also supported by the specification as filed. See, e.g., [0037] on page 11 and compounds I-26, I-46, I-49, I-52, I-57, I-59, I-61 and I-66 in Table 1.

The '549 patent only discloses a compound having an azepane ring directly linked to the 1,6-dihydropyrimidine-5-carbonitrile, wherein a phenyl ring is fused to the azepane ring and is not bound directly to the 1,6-dihydropyrimidine-5-carbonitrile. The compound disclosed in the '549 patent does not anticipate the instant claims because the azepane ring has 7 atoms and is therefore not encompassed by the definition of ring A. The fusion of the phenyl ring to the azepane ring does not cure this deficiency because it is not directly linked to the 1,6-dihydropyrimidine-5-carbonitrile. Thus, the '549 patent does not teach or suggest the claimed invention.

Allowable Subject Matter

Applicant acknowledges with appreciation the Examiner's indication that claims 6-8, 12 and 21-22 are allowable.

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Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying arguments, and allow the claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the Examiner contact the undersigned at his convenience.

Respectfully submitted,

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